Editorials

Managing Congestive Heart Failure Medically—What Have We Learned?

IN THE PAST TWO DECADES there has been considerable progress in understanding the epidemiology, pathophysiology, and management of congestive heart failure. Elsewhere in this issue of the journal, Arai and Greenberg have masterfully reviewed the pertinent literature and provided a useful outline of the medical management of chronic congestive heart failure.[1] Congestive heart failure is a clinical syndrome that can result from a variety of causes: valvular heart disease, pericardial disease, hypertension, coronary artery disease, and myocardial disease. Myocardial dysfunction is the most common denominator, however, and, thus, determining the nature and severity of myocardial dysfunction is essential for the rational management of heart failure.

Diastolic Failure

It is well established that both systolic and diastolic ventricular dysfunction can precipitate congestive heart failure. The hemodynamic abnormalities and signs and symptoms of congestive heart failure are similar whether heart failure results primarily from diastolic or systolic dysfunction. For clinical purposes, diastolic failure is defined as "impaired capacity of ventricles to fill without an inappropriate rise of atrial pressures." If this definition is accepted, a number of clinical conditions can be recognized in which abnormalities of ventricular filling appear to be the principal mechanism of congestive heart failure (Table 1).

The mechanism of impaired ventricular filling in these different clinical conditions is different, and understanding the various pathophysiologic mechanisms of diastolic dysfunction is necessary for rational management. For example, when abnormalities of left ventricular filling result from mitral valve obstruction or acute aortic and mitral valve regurgitation, correcting these mechanical defects is the most appropriate treatment. Myocardial ischemia, ventricular hypertrophy, and systemic hypertension, even without hypertrophy, are more frequent causes of left ventricular diastolic dysfunction. The precise mechanism for altered diastolic function in these clinical conditions is not known. Fibrosis, hypertrophy, and cellular disarray, however, may increase left ventricular passive chamber stiffness and thus enhance diastolic resistance to left ventricular filling. Ischemia, asynchrony, abnormal calcium flux, abnormal ventricular loading, and hypertrophy may also be associated with abnormal myocardial relaxation and impairment of ventricular filling. The diagnosis of diastolic dysfunction is best accomplished by determining the various indices of ventricular filling and relaxation: left ventricular end-diastolic pressure, ventricular compliance, peak filling rate, time to peak filling rate, atrial filling rate, peak negative change in pressure with respect to the change in time, and the time constant for ventricular relaxation. For clinical purposes, the demonstration of a normal or near-normal ejection fraction by echocardiography or radionuclide ventriculography strongly suggests that diastolic dysfunction is the principal cause of congestive heart failure. As myocardial ischemia and hypertrophy are two common causes of diastolic dysfunction, it is desirable to investigate for their presence and severity.

The incidence of diastolic dysfunction as the principal cause of congestive heart failure is difficult to estimate. Arai and Greenberg point out that although some studies have suggested that the prevalence of "diastolic failure" may be as high as 36%, in their experience it is closer to 5% to 10%.[1] Obviously, the methods of assessing diastolic function will influence the estimation of the incidence of diastolic failure. If the various indices of ventricular filling and relaxation function as mentioned earlier are used, it is likely that some abnormalities of ventricular filling will be detected in many patients with congestive heart failure. On the other hand, if the presence of a normal left ventricular ejection fraction is used as the principal criterion for the diagnosis of diastolic failure, the prevalence is likely to be much lower.

Pharmacotherapy for diastolic failure is largely empirical. Diuretics and nitrates are helpful in relieving symptoms, but an exessive reduction of the left ventricular filling pressure may be associated with a reduction in cardiac output and hypotension. Digitalis and other inotropic drugs are ineffective and are relatively contraindicated. A number of pharmacologic agents have the potential to improve diastolic function. In some patients with hypertrophic cardiomyopathy, calcium entry blocking agents, particularly verapamil, improve left ventricular compliance and filling characteristics. The relief of ischemia with nitrates, β-adrenergic blocking agents, and calcium entry blocking agents may be associated with improved left ventricular filling, compliance, and relaxation. Angiotensin-converting enzyme (ACE) inhibitors also improve diastolic function not only in hypertensive patients but also in patients with heart failure resulting from ischemic and nonischemic dilated cardiomyopathy. Thus, it is reasonable to consider the use of these pharmacologic agents in appropriate subsets of patients, although their effectiveness in improving the prognosis of patients with diastolic failure is uncertain (Table 2).

Systolic Failure

As Arai and Greenberg point out, a number of therapeutic options, some old and some new, are now available in the treatment of congestive heart failure that results primarily from left ventricular systolic dysfunction. We know that diuretics are an effective and essential therapy for the relief of congestive symptoms. The reduction of systemic and pulmonary venous pressure is the predominant mechanism for these beneficial effects. We have also learned that long-term diuretic therapy does not increase cardiac output and, thus, symptoms related to low cardiac output are unlikely to be ameliorated with diuretic therapy alone. Furthermore, the long-term use of large doses of diuretics frequently induces renal failure and activates the renin-angiotensin-aldosterone system, which may increase left ventricular afterload

TABLE 1.—*Congestive Heart Failure Due to Diastolic Dysfunction*

Mitral valve obstruction
Constrictive pericarditis
Restrictive cardiomyopathy
Acute volume overload (aortic regurgitation, mitral regurgitation)
Myocardial ischemia
Ventricular hypertrophy
Hypertension

and produce adverse effects on cardiac performance. Thus, diuretic therapy alone cannot be recommended for the long-term management of heart failure.

Arai and Greenberg elegantly discuss the controversies regarding long-term digitalis therapy in the management of patients with heart failure in sinus rhythm.[1] The results of a number of prospective controlled studies indicate that long-term digitalis therapy is indeed effective in improving left ventricular ejection fraction, the clinical state, and exercise tolerance in the majority of patients with chronic heart failure, provided heart failure results from impaired systolic function.[2,3] It is uncertain, however, whether digitalis is effective in patients with depressed systolic function with no or minimal symptoms. Thus, at present long-term digitalis therapy can be recommended in almost all symptomatic patients with chronic heart failure with a reduced left ventricular ejection fraction, provided there is no overt contraindication (severe renal failure, digitalis toxicity).

Is diuretic and digitalis therapy sufficient for the effective management of chronic heart failure? A number of well-controlled prospective studies have now shown that the addition of direct-acting vasodilators—hydralazine hydrochloride and isosorbide dinitrate combination—or of ACE inhibitors to digitalis and diuretics not only improves the clinical state but also reduces mortality. In patients with mild to moderate heart failure, a 38% reduction in one-year mortality has been reported with the use of hydralazine-isosorbide dinitrate.[4] In patients with more severe heart failure (New York Heart Association class IV), ACE inhibitor therapy decreased the one-year mortality by 31%.[5] Thus, based on available information, the addition of hydralazine-isosorbide dinitrate or ACE inhibitors seems appropriate for the management of virtually all cases of symptomatic chronic heart failure. One practical question needs to be considered regarding vasodilator therapy for heart failure—whether hydralazine-isosorbide dinitrate or ACE inhibitors should be given preference. Angiotensin-converting enzyme inhibitors appear to provide some advantage over hydralazine-isosorbide dinitrate in that they decrease myocardial oxygen consumption more consistently. A favorable change in neuroendocrine abnormalities such as a reduction in catecholamines and angiotensin II and aldosterone levels occurs with the use of ACE inhibitors.[6,7] In addition, they have the potential to prevent ventricular remodeling and dilatation.[8] Thus, my own bias is to use ACE inhibitors in preference to hydralazine-isosorbide dinitrate, provided they are well tolerated and do not produce serious adverse effects.

Is there any other therapy for patients refractory or intolerant to vasodilators and ACE inhibitors? At present the alternatives are extremely limited, except for cardiac transplantation, which undoubtedly improves the prognosis in patients with end-stage heart failure. Intermittent intravenous inotropic therapy with dobutamine hydrochloride or phosphodiesterase inhibitors (amrinone, enoximone, milrinone) can improve the clinical state in some patients, but the duration of beneficial response is variable and the prognosis does not appear to be influenced by such therapy. A few, mainly uncontrolled studies have suggested that amiodarone and β-adrenergic blocking agents may be of benefit in patients with dilated cardiomyopathy.[9,10] Clinical experience with such therapy, however, is too limited to allow for an assessment of the effectiveness of these agents in the routine management of chronic heart failure. It is apparent that many investigations will be required to identify more appropriate and more effective pharmacotherapy for patients with refractory heart failure, without which the outlook will remain dismal. Nevertheless, based on available information, a rational therapeutic approach can be outlined for the management of systolic heart failure (Table 3).

TABLE 2.—*Outline of Management of Diastolic Failure*

Problem	*Therapy*
Congestive symptoms	Moderate dose of diuretics and nitrates
Diastolic dysfunction in hypertensive patients	Antihypertensive agents, particularly calcium entry blocking agents, ACE inhibitors, and certain β-blockers
Diastolic dysfunction resulting from ischemia	Nitrates, β-blockers, calcium entry blocking agents, revascularization
Diastolic dysfunction due to hypertrophy	Calcium entry blocking agents, ACE inhibitors
Diastolic dysfunction in hypertrophic cardiomyopathy	Calcium entry blocking agents, particularly verapamil

ACE = angiotensin-converting enzyme

TABLE 3.—*Outline of Management of Systolic Failure*

Problem	*Therapy*
Minimal or no symptoms; postinfarction; left ventricular dysfunction	? ACE inhibitors
Mild to moderately severe heart failure	Digitalis, diuretics, and hydralazine-nitrates or ACE inhibitors
Severe heart failure	Digitalis, diuretics, and ACE inhibitors
Severe heart failure refractory to ACE inhibitors	Intermittent dobutamine or phosphodiesterase inhibitors, newer inotropic agents, amiodarone or β-blockers in selected patients; cardiac transplantation, if possible

ACE = angiotensin-converting enzyme

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Consider the Alternatives

CONSIDERABLE FUROR HAS ARISEN in the wake of the first report in the world "consistent with transmission of human immunodeficiency virus to a patient during an invasive dental procedure, although the possibility of another source of infection cannot be entirely excluded."[1] The report raises numerous issues such as the modes of transmission of human immunodeficiency virus (HIV), the reliability of retrospective epidemiologic investigations, and the usefulness of DNA sequencing in case analyses of this type. For physicians, part of the debate has centered on informed consent. That is, should patients be informed that their physician is HIV antibody-positive or has the acquired immunodeficiency syndrome (AIDS)? Scenarios have descended to the level of, "Let's make a deal. I'll tell you if you tell me." The issue is much broader than HIV and games.

The hepatitis B virus, for example, is far more prevalent than HIV and is also blood-borne. Hepatitis B virus clearly has been transmitted, very rarely, to patients in gynecologic and dental settings.[2,3] (Never forget that although hepatitis B is a disease preventable by recombinant vaccine, 200 to 300 health care workers, including physicians, die *every year* in the United States of hepatitis B contracted at work. If health care workers were successfully immunized, they would not die of hepatitis B nor transmit it.) Should patients be told their physician's hepatitis B status?

In addition to the possibility that infections might be transmitted by a physician (or dentist, laboratory technician, or nurse), the question of impairment must be addressed. A physician with AIDS may be too sick, too tired, or too demented to have the clarity, stamina, or judgment necessary to practice good medicine. A physician with hepatitis B may be in the same situation. Similarly, but aside from infectious diseases, a physician with a diagnosis such as cancer, cardiovascular disease, or manic-depressive disorder may be unable to "practice medicine with reasonable skill and safety to patients" (AMA Council on Mental Health, American Medical Association, 1972). A physician with an active addiction or in early recovery also may be impaired.

What should we tell our patients? Our colleagues? Our staff? Should physicians announce their HIV status or hepatitis B virus status or their potentially mind-damaging, life-threatening diagnoses or their chemical dependencies? Should they discuss their treatment status? Should consideration be given to physicians' privacy as well as patients' privacy?

The human immunodeficiency virus yet again has presented our profession with a challenge that goes far beyond the obvious. In this instance, the issue transcends disclosure of, or testing for, HIV infection. No one wants to die of AIDS nor transmit the virus. No one wants to die of hepatitis B nor transmit that virus. No one wants to damage patients or family because of impairment for any reason. We want to serve. What, if anything, should we tell our patients about our ability to do so? All or none? Case by case? Publicly or privately? What is best for patients? And physicians? And our profession? Our decisions must be based on science and prudence, compassion and reason. Thorough and unbiased education—of ourselves, our patients, and the public—will assure that we will deal effectively with misinformation, panic, prejudice, and fear. We must consider, and choose, the best alternatives.

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